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nGPCR-60. Table 1 below identifies the novel gene sequence nGPCR-x designation, the SEQ ID NO: of the gene sequence, the SEQ ID NO: of the polypeptide encoded thereby, and the U.S. Provisional Application in which the gene sequence has been disclosed.

Table 1

nGPCR	Nucleotide Sequence (SEQ ID NO:)	Amino acid Sequence (SEQ ID NO:)	Originally filed in:	nGPCR	Nucleotide Sequence (SEQ ID NO:)	Amino acid Sequence (SEQ ID NO:)	Originally filed in:
1	11	2	<u>A</u>	32	39	40	В
1	73	74	E	33	41	42	С
3	3	4	Α	34	43	44	C
3	185	186	P	35	45	46	С
4	5	6	A	36	47	48	C
5	7	8	A	37	49	50	С
5	75	76	F	38	51	52	С
9	9	10	A	- 40	53	54	С
9	77	78	G	40	83	84	j
11	11	12	Α	41	55	56	С
11	79	80	Н	53	57	58	D
12	13	14	A	54	59	60	D
14	15	16	A	54	85	86	K
15	17	18	A	55	61	62	D
18	19	20	Α	56	63	64	D
16	21	22	В	56	87	88	L
16	81	82	l	56	89	90	M
17	23	24	В	57	65	66	D
20	25	26	В	58	67	68	D
21	27	28	В	58	91	92	N
22	29	30	В	58	93	94	0
24	31	32	В	59	69	70	D
27	33	34	В	60	71	72	D
28	35	36	В				
31	37	38	В				

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A= Ser. No. 60/165,838	I= Ser. No. 60/186,530
B= Ser. No. 60/166,071	J= Ser. No. 60/207,094
C= Ser. No. 60/166,678	K= Ser. No. 60/203,111
D= Ser. No. 60/173,396	L= Ser. No. 60/190,310
E= Ser. No. 60/184,129	M= Ser. No. 60/201,190
F= Ser. No. 60/188,114	N= Ser. No. 60/185554
G= Ser. No. 60/185,421	O= Ser. No. 60/190,800
H= Ser. No. 60/186,811	P= Ser. No. 60/198,568
	B= Ser. No. 60/166,071 C= Ser. No. 60/166,678 D= Ser. No. 60/173,396 E= Ser. No. 60/184,129 F= Ser. No. 60/188,114 G= Ser. No. 60/185,421

When a specific nGPCR is identified (for example nGPCR-5), it is understood that only that specific nGPCR is being referred to.

As described in Example 4 below, the genes encoding nGPCR-1 (nucleic acid sequence SEQ ID NO: 1, SEQ ID NO: 73, amino acid sequence SEQ ID NO: 2, SEQ ID NO:74), nGPCR-9 (nucleic acid sequence SEQ ID NO:9, SEQ ID NO:77, amino acid sequence SEQ ID NO:10, SEQ ID NO:78), nGPCR-11 (nucleic acid sequence

SEQ ID NO:11, SEQ ID NO:79, amino acid sequence SEQ ID NO:12, SEQ ID NO:80), nGPCR-16 (nucleic acid sequence SEQ ID NO: 21, SEQ ID NO:81, amino acid sequence SEQ ID NO: 22, SEQ ID NO:82), nGPCR-40 (nucleic acid sequence SEQ ID NO:53, SEQ ID NO:83, amino acid sequence SEQ ID NO:54, SEQ ID NO:84), nGPCR-54 (nucleic acid sequence SEQ ID NO:59, SEQ ID NO:85, amino acid sequence SEQ ID NO:60, SEQ ID NO: 86), nGPCR-56 (nucleic acid sequence SEQ ID NO:63, SEQ ID NO:87, SEQ ID NO:89, amino acid sequence SEQ ID NO:64, SEQ ID NO: 88, SEQ ID NO:90), nGPCR-58 (nucleic acid sequence SEQ ID NO:67, SEQ ID NO:91, SEQ ID NO:93, amino acid sequence SEQ ID NO:68, SEQ ID NO: 92, SEQ ID NO:94) and nGPCR-3 (nucleic acid sequence SEQ ID NO:3, SEQ ID NO:185, amino acid sequence SEQ ID NO:4, SEQ ID NO: 186) have been detected in brain tissue indicating that these n-GPCR-x proteins are neuroreceptors.

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The invention provides purified and isolated polynucleotides (e.g., cDNA, genomic DNA, synthetic DNA, RNA, or combinations thereof, whether single- or double-stranded) that comprise a nucleotide sequence encoding the amino acid sequence of the polypeptides of the invention. Such polynucleotides are useful for recombinantly expressing the receptor and also for detecting expression of the receptor in cells (e.g., using Northern hybridization and in situ hybridization assays). Such polynucleotides also are useful in the design of antisense and other molecules for the suppression of the expression of nGPCR-x in a cultured cell, a tissue, or an animal; for therapeutic purposes; or to provide a model for diseases or conditions characterized by aberrant nGPCR-x expression. Specifically excluded from the definition of polynucleotides of the invention are entire isolated, non-recombinant native chromosomes of host cells. A preferred polynucleotide has the sequence of the sequence set forth in odd numbered sequences ranging from SEQ ID NO: 1 to SEQ ID NO: 93 and SEQ ID NO: 185, which correspond to naturally occurring nGPCR-x sequences. It will be appreciated that numerous other polynucleotide sequences exist that also encode nGPCR-x having the sequence set forth in even numbered sequences ranging from SEQ ID NO: 2 to SEQ ID NO: 94 and SEQ ID NO: 186, due to the well-known degeneracy of the universal genetic code.

The invention also provides a purified and isolated polynucleotide comprising a nucleotide sequence that encodes a mammalian polypeptide, wherein the polynucleotide hybridizes to a polynucleotide having the sequence set forth in odd numbered sequences ranging from SEQ ID NO: 1 to SEQ ID NO: 93 and SEQ ID

774; Ubl & Reiser. (1997) Glia 21:361-369; Grabham & Cunningham (1995) J Neurochem 64:583-591.

nGPCR-x receptor activation may mediate neuronal and astrocyte apoptosis and prevention of neurite outgrowth. Inhibition would be beneficial in both chronic and acute brain injury. See, e.g., Donovan et al. (1997) J Neurosci 17:5316-5326; Turgeon et al (1998) J Neurosci 18:6882-6891; Smith-Swintosky et al. (1997) J Neurochem 69:1890-1896; Gill et al. (1998) Brain Res 797:321-327; Suidan et al. (1996) Semin Thromb Hemost 22:125-133.

The attached Sequence Listing contains the sequences of the polynucleotides and polypeptides of the invention and is incorporated herein by reference in its entirety.

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As described above and in Example 4 below, the genes encoding nGPCR-1 (nucleic acid sequence SEQ ID NO: 1, SEQ ID NO: 73, amino acid sequence SEQ ID NO: 2, SEQ ID NO:74), nGPCR-9 (nucleic acid sequence SEQ ID NO:9, SEQ ID NO:77, amino acid sequence SEQ ID NO:10, SEQ ID NO:78), nGPCR-11 (nucleic acid sequence SEQ ID NO:11, SEQ ID NO:79, amino acid sequence SEQ ID NO:12, SEQ ID NO:80), nGPCR-16 (nucleic acid sequence SEQ ID NO: 21, SEQ ID NO:81, amino acid sequence SEQ ID NO: 22, SEQ ID NO:82), nGPCR-40 (nucleic acid sequence SEQ ID NO:53, SEQ ID NO:83, amino acid sequence SEQ ID NO:54, SEQ ID NO:84), nGPCR-54 (nucleic acid sequence SEQ ID NO:59, SEQ ID NO:85, amino acid sequence SEQ ID NO:60, SEQ ID NO: 86), nGPCR-56 (nucleic acid sequence SEQ ID NO:63, SEQ ID NO:87, SEQ ID NO:89, amino acid sequence SEQ ID NO:64, SEQ ID NO: 88, SEQ ID NO:90), nGPCR-58 (nucleic acid sequence SEQ ID NO:3, SEQ ID NO:185, amino acid sequence SEQ ID NO:4, SEQ ID NO: 186) have been detected in brain tissue indicating that these n-GPCR-x proteins are neuroreceptors. The identification of modulators such as agonists and antagonists is therefore useful for the identification of compounds useful to treat neurological diseases and disorders. Such neurological diseases and disorders, including but are not limited to, schizophrenia, affective disorders, ADHD/ADD (i.e., Attention Deficit-Hyperactivity Disorder/Attention Deficit Disorder), and neural disorders such as Alzheimer's disease, Parkinson's disease, migraine, and senile dementia as well as depression, anxiety, bipolar disease, epilepsy, neuritis, neurasthenia, neuropathy, neuroses, and the like.

ACTCCTCGGTGCTGTTCAGGTGTTTCTGGAATGGATCTTCTAGTTTCTGCTGGTAGATCCAGGAAGCATTCTGAAGTTTTTCCATCCCTGA

The following amino acid sequence <SEQ ID NO. 18> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 17:

SGMEKLQNASWIYQQKLEDPFQKHLNSTEEYLAFLCGPRRSHFFLPVSVVYVPIFVVGVIGNVLVCLVILQHQ AMKTPNTYYLFSLAVSDLLVLLLGMPLEVYEMWRNYPFLFGPVGCYFKTALFETVCFASILSITTVSVERYVA ILHPFRAKLQSTRRRALRILGIVWGFSVLFSLPNTSIHGIKFHYFPNGSLVPGSATCTVIKPMWIYNFIIQVT SFLFYLLPMTVISVLYYLMALRVSIAGVAG

The following DNA sequence beGPCR-seq18 <SEQ ID NO. 19> was identified in H. sapiens:

The following amino acid sequence <SEQ ID NO. 20> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 19:

IKM1FAIVQIIGFSNSICNPIVYAFMNENFKKNVLSAVCYCIVNKTFSPAQRHGNSGITMMRKKAKFSLRENP

The following DNA sequence beGPCR-seq16 <SEQ ID NO. 21> was identified in H. sapiens:

The following amino acid sequence <SEQ ID NO. 22> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 21:

VSYSGAFSPPGDFPSMPGHNTSRNSSCDPIVTPHLISLYFIVLIGGLVGVISILFLLVKMNTRSVTTMAVINL VVVHSVFLLTVPFRLTYLIKKTWMFGLPFCKFVSAMLHIHMYLTVPILCGDPGHQIPHLLQVQRQSGILQKTA CCG

The following DNA sequence beGPCR-seq17<SEQ ID NO. 23> was identified in H. sapiens:

The following amino acid sequence <SEQ ID NO. 24> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 23:

CEYLFESWGIRLAVWAIVLLSVLCNGLVLLTVFAGGPAPLPPVKFVVGAIAGANTLTGISCGLLASVDALTLV S

The following DNA sequence beGPCR-seq20 <SEQ ID NO. 25> was identified in H. sapiens:

The following amino acid sequence <SEQ ID NO. 78> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 77:

MESGLLRPAPVSEVIVLHYNYTGKLRGARYQPGAGLRADAVVCLAVCAFIVLENLAVLLVLGRHPRFHAPMFL
LLGSLTLSDLLAGAAYAANILLSGPLTLKLSPALWFAREGGVFVALTASVLSLLAIALERSLTMARRGPAPVS
SRGRTLAMAAAAWGVSLLLGLLPALGWNCLGRLDACSTVLPLYAKAYVLFCVLAFVGILAAICALYARIYCQV
RANARRLPARPGTAGTTSTRARRKPRSLALLRTLSVVLLAFVACWGPLFLLLLDVACPARTCPVLLQADPFL
GLAMANSLLNPIIYTLTNRDLRHALLRLVCCGRHSCGRDPSGSQQSASAAEASGGLRRCLPPGLDGSFSGSER
SSPQRDGLDTSGSTGSPGAPTAARTLVSEPAAD

The following DNA sequence nGPCR-11 <SEQ ID NO. 79> was identified in H. sapiens:

The following amino acid sequence <SEQ ID NO. 80> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 79:

MYNGSCCRIEGDTISQVMPPLLIVAFVLGALGNGVALCGFCFHMKTWKPSTVYLFNLAVADFLLMICLPFRTD
YYLRRRHWAFGDIPCRYGLFTLAMNRAGSIVFLTVVAADRYFKVVHPHHAVNTISTRVAAGIVCTLWALVILG
TYYLLLENHLCVQETAVSCESFIMESANGWHDIMFQLEFFMPLGIILFCSFKIVWSLRRRQQLARQARMKKAT
RFIMVVAIVFITCYLPSVSARLYFLWTVPSSACDPSVHGALHITLSFTYMNSMLDPLVYYFSSPSFPKFYNKL
KICSLKPKQPGHSKTQRPEEMPISNLGRRSCISVANSFQSQSDGQWDPHIVEWH

The following DNA sequence nGPCR-16 <SEQ ID NO. 81> was identified in H. sapiens:

anxiety, bipolar disease, epilepsy, neuritis, neurasthenia, neuropathy, neuroses, and the like. Use of nGPCR-x modulators, including nGPCR-x ligands and anti-nGPCR-x antibodies, to treat individuals having such disease states is intended as an aspect of the invention.

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EXAMPLE 4: TISSUE EXPRESSION PROFILING

Tissue specific expression of the cDNAs encoding nGPCR-1, nGPCR-3, nGPCR-9, nGPCR-11, nGPCR-16, nGPCR-40, nGPCR-54, nGPCR-56, and nGPCR-58 was detected using a PCR-based system. Tissue specific expression of cDNAs encoding nGPCR-x may be accomplished using similar methods.

Primers were synthesized by Genosys Corp., The Woodlands, TX. PCR reactions were assembled using the components of the Expand Hi-Fi PCR SystemTM (Roche Molecular Biochemicals, Indianapolis, IN).

nGPCR-1

The RapidScanTM Gene Expression Panel was used to generate a comprehensive expression profile of the putative GPCR in human tissues. Human tissues in the array may include: brain, heart, kidney, spleen, liver, colon, lung, small intestine, muscle, stomach, testis, placenta, salivary gland, thyroid, adrenal gland, pancreas, ovary, uterus, prostate, skin, PBL, bone marrow, fetal brain, fetal liver. Human brain regions in the array may include: frontal lobe, temporal lobe, cerebellum, hippocampus, substantia nigra, caudate nucleus, amygdala, thalamus, hypothalamus, pons, medulla and spinal cord.

Expression of the nGPCR-1 in the various tissues was detected by using PCR primers designed based on the available sequence of the receptor that will prime the synthesis of a 212bp fragment in the presence of the appropriate cDNA. The forward primer was:

GCTCAACCCACTCATCTATGCC (SEQ ID NO: 97), and the reverse primer was:

AAACTTCTCTGCCCTTACCGTC (SEQ ID NO: 98)

The PCR reaction mixture was added to each well of the PCR plate. The plate was placed in a GeneAmp PCR9700 PCR thermocycler (Perkin Elmer Applied Biosystems). The plate was then exposed to the following cycling parameters: Presoak 94°C for 3 min; denaturation at 94°C for 30 seconds; annealing at primer T_m for

disease, epilepsy, neuritis, neurasthenia, neuropathy, neuroses, and the like. Use of nGPCR-11 modulators, including nGPCR-11 ligands and anti-nGPCR-11 antibodies, to treat individuals having such disease states is intended as an aspect of the invention.

Expression of nGPCR-11 in the thyroid gland, indicates that agonists or antagonists could be of use in the treatment of thyroid dysfunction such as thyreotoxicosis and myxoedema. They could also be of use in the stimulation of thyroid hormone release leading to overall increase in metabolic rate and weight reduction. The expression of nGPCR-11 in liver and muscle indicate a use for agonists or antagonists in regulation of glucose metabolism applicable in diabetes type II.

nGCPR-16

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The RapidScanTM Gene Expression Panel was used to generate a comprehensive expression profile of the putative GPCR in human tissues. Human tissues in the array included, *inter alia*: brain, heart, kidney, spleen, liver, colon, lung, small intestine, muscle, stomach, testis, placenta, salivary gland, thyroid, adrenal gland, pancreas, ovary, uterus, prostate, skin, PBL, bone marrow, fetal brain, fetal liver. Human brain regions in the array included, *inter alia*: frontal lobe, temporal lobe, cerebellum, hippocampus, substantia nigra, caudate nucleus, amygdala, thalamus, hypothalamus, pons, medulla and spinal cord.

Expression of nGPCR-16 in the various tissues was detected by using PCR primers designed based on the available sequence of the receptor that will prime the synthesis of a 205bp fragment in the presence of the appropriate cDNA. The forward primer used to detect expression of nGPCR-16 was:

5' CAGCCCAAACATCCAAGTC 3'. (SEQ ID NO: 113). The reverse primer used to detect expression of nGPCR-16 was:

5' ACCCCACTTAATCAGCCTC 3'(SEQ ID NO: 114).

For detection of expression within brain regions, the same primer set was used with the Human Brain Rapid ScanTM Panel (OriGene Technologies, Rockville, MD). This panel represents serial dilutions over a 2 log range of first strand cDNA from the following brain regions arrayed in a 96 well format: frontal lobe, temporal lobe, cerebellum, hippocampus, substantia nigra, caudate nucleus, amygdala, thalamus, hypothalamus, pons, medulla and spinal cord.

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180

240

300

360

420

447

<213> H.Sapiens <400> 21 qccacaqcat gcaqttttct gtagaattcc actttgtctt tgcacttgaa gaaqatgaqq tatctgqtqa ccaqqatcac cacatagaat aggaaccgtq aggtacatgt qqatqtqcaq catggcactc acaaatttgc agaagggcag cccaaacatc caagtcttct tgatgaggta ggtcaagcga aatggcactg tcagcagaaa aacgctgtgg accaccacca agttaatgac cgccatggtg gtcactgacc gggtgttcat tttcaccagg aggaaaagaa tggaaatgac acccaccage cegecaataa geactatgaa gtagaggetg attaagtggg gtgtcactat aggategeaa gaggaattee tggaggtatt gtggeeagge atacttggga agteacetgg aggagaaaaa gcaccagagt aactgac <210> 22 <211> 149 <212> PRT <213> H.Sapiens <400> 22 Val Ser Tyr Ser Gly Ala Phe Ser Pro Pro Gly Asp Phe Pro Ser Met Pro Gly His Asn Thr Ser Arg Asn Ser Ser Cys Asp Pro Ile Val Thr Pro His Leu Ile Ser Leu Tyr Phe Ile Val Leu Ile Gly Gly Leu Val Gly Val Ile Ser Ile Leu Phe Leu Leu Val Lys Met Asn Thr Arg Ser Val Thr Thr Met Ala Val Ile Asn Leu Val Val Val His Ser Val Phe 70 Leu Leu Thr Val Pro Phe Arg Leu Thr Tyr Leu Ile Lys Lys Thr Trp Met Phe Gly Leu Pro Phe Cys Lys Phe Val Ser Ala Met Leu His Ile His Met Tyr Leu Thr Val Pro Ile Leu Cys Gly Asp Pro Gly His Gln

Ile Pro His Leu Leu Gln Val Gln Arg Gln Ser Gly Ile Leu Gln Lys

Thr Ala Cys Cys Gly 145

<210> 23 <211> 222

130

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- Met Asn Arg Ala Gly Ser Ile Val Phe Leu Thr Val Val Ala Ala Asp 100 105 110
- Arg Tyr Phe Lys Val Val His Pro His His Ala Val Asn Thr Ile Ser 115 120 125
- Thr Arg Val Ala Ala Gly Ile Val Cys Thr Leu Trp Ala Leu Val Ile 130 135 140
- Leu Gly Thr Val Tyr Leu Leu Leu Glu Asn His Leu Cys Val Gln Glu 145 150 150 160
- Thr Ala Val Ser Cys Glu Ser Phe Ile Met Glu Ser Ala Asn Gly Trp 165 170 175
- His Asp Ile Met Phe Gln Leu Glu Phe Phe Met Pro Leu Gly Ile Ile 180 185 190
- Leu Phe Cys Ser Phe Lys Ile Val Trp Ser Leu Arg Arg Arg Gln Gln 195 200 205
- Leu Ala Arg Gln Ala Arg Met Lys Lys Ala Thr Arg Phe Ile Met Val 210 215 220
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- Leu Tyr Phe Leu Trp Thr Val Pro Ser Ser Ala Cys Asp Pro Ser Val 245 250
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